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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/596,086	06/16/2000	Elfi Biedermann	69054	3172.

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 11/18/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/596,086

Applicant(s)
BIEDERMANN et al.

Examiner
Brenda Coleman

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1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 9, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-54 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

Claims 32-54 are pending in the application.

This action is in response to applicants' amendment filed September 9, 2002. Claims 1-31 have been canceled and claims 32-54 are newly added.

Response to Amendment

Applicants' arguments filed September 9, 2002 have been fully considered with the following effect:

1. The applicant's amendments are sufficient to overcome the rejection as being drawn to an improper Markush group of the last office action which is hereby **withdrawn**.
2. With regards to the objection to the Information Disclosure Statement the applicants failed to comment.

The information disclosure statement filed January 4, 2001 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the first citation under the heading OTHER DOCUMENTS is **incomplete and not in the English language**. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on

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the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

It is also noted that there are three Chemical Abstracts listed under the heading OTHER DOCUMENTS where there is no indication what the chemical abstract number is and it is not known what is meant by the Rote Liste, 1997 which is the last citation under the heading OTHER DOCUMENTS.

3. With regards to the objection to the abstract of the disclosure, the applicants failed to comment.

The abstract of the disclosure is objected to because the content of the abstract is of different scope than the claims. Correction is required. See MPEP § 608.01(b).

4. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 8-31, labeled paragraph 5), the applicants failed to comment, however, in view of the amendment canceling claims 8-31 the rejection is herein maintained with respect to the corresponding newly added claims.

Claims 37-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these

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claims. Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689. The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the “tumor” category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

5. The applicant’s amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled b)-g), i)-k), m)-v) and x)-bf) which are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled a), h), l) and w) of the last office action, the applicant’s amendments and remarks have been fully considered but they are not persuasive.

- a) The applicants failed to comment on the rejection of claim 1 (and claims dependent thereon) with respect to the plurality of amides which is herein maintained with respect to the newly added claims.
- h) The applicants failed to comment on the rejection of claims 3-5 (and claims dependent thereon) with respect to the plurality of compounds which is herein maintained with respect to the newly added claims.

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- l) The applicants' stated that "when the claims refer to methylene units they now indicate which compounds the methylene units are a part of". The definition of D in newly added claim 35 is such that one or two methylene units in the C₃-C₈-alkylene, C₃-C₈-alkenylene or C₃-C₈-alkynylene are isosterically replaced. However, claim 35 depends on claim 34 where the definition of D is limited to only one methylene unit, i.e. the definition of D in newly added claim 34 is such that a methylene unit is isosterically replaced.
- w) The applicants' stated that "nucleofuge is known in the art as a leaving group. However, several attempts have been made using every available reference to find a definition for nucleofuge. It is not seen how one of ordinary skill in the art would understand what nucleofuge is, if a definition is not readily available.

Claims 32-36 and 50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For reasons of record and stated above.

6. With regards to the 35 U.S.C. § 102, anticipation rejection of claims 1-4, 7-11, 29 and 31 in the last office action, the applicants stated that "the claims as presented herewith do not define compounds as described in the Ishihara reference". However, example 3n is a species which is embraced by the instant claims. Ishihara teaches the compounds, compositions, process of

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preparing and method of use of the instant invention where R^1 , R^2 and R^3 are hydrogen, A is -CH=CH-, D is $(CH_2)_5$ and G is -N(C₂H₅)-CH₂-phenyl.

Claims 32-34, 37 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishihara et al., Chem. Pharm Bull. For reasons of record and stated above.

In view of the amendment dated September 9, 2002, the following new grounds of rejection apply:.

Claim Rejections - 35 USC § 112

The following is as a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain as a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 32-34 and 37-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such as a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to the definition of G^4 where the residues are pyridyl-A-C(O)- and NR^{11} -C(O)-Y-(CR⁹R¹⁰)_m-R⁸ is not described in the specification.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 32-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claim 32 is vague and indefinite in that it is not known what is meant by pyridyl**akane** or pyridyl**akene**.
- b) Claims 32 and 37-54 is vague and indefinite in that it is not known what is meant by C₃-C₈-cycloalkylo**Zy** in the definition of R¹.
- c) Claims 32 and 37-54 are vague and indefinite in that it is not known what is meant by the definition of R⁷ where R⁷ is defined as R⁷ has the same as R⁶. The same what?
- d) Claims 32 and 37-50 are vague and indefinite in that it is not known what is meant by the definition of R¹¹ where R¹¹ has the same meanings (plural) as R⁴. R¹¹ has only one definition.
- e) Claims 32-34, 37-50 and 52 are vague and indefinite in that it is not known what is meant by the definition of G⁴ such that there is no indication where the point of attachment is for the two moieties.
- f) Claims 32-34, 37-50 and 52-54 are vague and indefinite in that it is not known what is meant by the reference to the grouping NR⁸R⁹.

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- g) Claims 32, 37-50 and 52 are vague and indefinite in that it is not known what is meant by the definition of R^{12} where the linkage can occur **either** over an aromatic ring.
- h) Claims 32, 37-50 and 52 are vague and indefinite in that it is not known what is meant by the definition of G^6 such that there is no indication where the point of attachment is for the moiety.
- i) Claims 32-34, 37-50 and 52 are vague and indefinite in that it is not known what is meant by the definition of X where X has the above meanings (plural). X has only one definition.
- j) Claims 32-34 and 37-54 are vague and indefinite in that it is not known what is meant by the list of substituents for the ring system $-NR^8R^9$, since the claim no longer contains a ring system $-NR^8R^9$.
- k) Claims 32 and 37-54 are vague and indefinite in that it is not known what is meant by **benyloxy** and **benyloxycarbonyl** in the list of substituents for the aromatic ring systems.
- l) Claim 33 is vague and indefinite in that the definition of R^2 is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and".
- m) Claim 33 is vague and indefinite in that it is not known what is meant by "naphthyl" and "dihydronaphthyl" in the definition of R^8 .

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- n) Claim 33 is vague and indefinite in that the definition of R^8 is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and".
- o) Claim 33 recites the limitation "benzofuryl, dihydrobenzofuryl, benzothienyl,oxodihydropyridobenzothiazepinyl, bound directly or over a methylene group" in the definition of R^8 . There is insufficient antecedent basis for this limitation in the claim.
- p) Claims 33 and 34 recite the limitation " C_3 - C_8 -cycloalkyl" in the definition of R^9 . There is insufficient antecedent basis for this limitation in the claim.
- q) Claims 33 and 34 are vague and indefinite in that the definition of R^9 is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and".
- r) Claim 33 recites the limitation "benzofuryl, benzothienyl, indolyl, indolinyl,dihydrobenzoisoquinolinyl, phenothiazinyl" in the definition of R^9 . There is insufficient antecedent basis for this limitation in the claim.
- s) Claims 33 and 34 recite the limitation "or whereby the grouping $=CR^8R^9$ can also be a ring systemdihydropyridobenzothiepinyl" in the definition of G^2 . There is insufficient antecedent basis for this limitation in the claim.

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- t) Claim 33 recites the limitation "indolyl, benzothienyl and quinolinyl" in the definition of R¹². There is insufficient antecedent basis for this limitation in the claim.
- u) Claims 34 and 35 are vague and indefinite in that it is not known what is meant by trifluoromethyl in the definition of R¹.
- v) Claim 34 is vague and indefinite in that the definition of A is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and".
- w) Claim 34 is vague and indefinite in that it is not known what is meant by "naphthyl" in the definition of R⁸.
- x) Claim 34 is vague and indefinite in that the definition of R⁸ is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and".
- y) Claim 34 recites the limitation "benzofuryl, benzothienyl, indolyl, indolinyl,dihydrodibenzooxazepinyl" in the definition of R⁸. There is insufficient antecedent basis for this limitation in the claim.
- z) Claim 34 is vague and indefinite in that it is not known what is meant by naphthyl anthryl in the definition of R⁹.

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- aa) Claim 34 recites the limitation "benzofuryl, benzothienyl, indolyl, benzooxazolyl,benzoisothiazolyl, benzoimidazolyl and benzotriazolyl" in the definition of R⁹.
There is insufficient antecedent basis for this limitation in the claim.
- ab) Claim 34 recites the limitation "benzothienyl and quinoliny" in the definition of R¹². There is insufficient antecedent basis for this limitation in the claim.
- ac) Claim 34 is vague and indefinite in that it is not known what is meant by residues in the definition of the substituents for Group G at the end of the claim.
- ad) Claim 35 recites the limitation "or OCH₂, SCH₂" in the definition of A. There is insufficient antecedent basis for this limitation in the claim.
- ae) Claim 35 is vague and indefinite in that the definition of A is not written as a proper Markush grouping. Selected from the group consisting of should terminate with an "and" not an "or".
- af) Claim 35 recites the limitation "**cyclopentyl**phenylmethylene, **cyclohexyl**phenylmethyl, **cyclohexyl**hydroxyphenylmethyl" in the definition of G.
There is insufficient antecedent basis for this limitation in the claim.
- ag) Claim 35 recites the limitation "diphenyle**thyl**, diphenylhydroxy**ethyl**, diphenyle**thylene**, triphenyle**thyl**, triphenylhydroxy**ethyl** or triphenyle**thylene**" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.

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- ah) Claim 35 is vague and indefinite in that it is not known what is meant by triphenylhydroxyethyl, which is valence satisfied.
- ai) Claim 35 recites the limitation "tetrahydronaphthylidene, fluoroenyl, hydroxyfluoroenyl, fluoroenylidene, tetrahydrobenzocyclohexenylidene or dihydrodibenzocycloheptenylidene" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.
- aj) Claim 35 recites the limitation "phenyl-thienylmethyl, phenyl-thienylhydroxymethyl, phenyl-.....benzotriazolyl" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.
- ak) Claim 35 recites the limitation "cyclohexylphenylamino" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.
- al) Claim 35 is vague and indefinite in that it is not known what is meant by biphenylamino in the definition of G.
- am) Claim 35 recites the limitation "N-indolyl, N-isoindolyl,N-dihydrodibenzoazepinyl" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.
- an) Claim 35 recites the limitation "furoylacrylamino, oxofluoroenylcarbonylamino, furoylamino, diphenylfurylaminocarbonylamino, indolyl-N-carbonylamino,.....dihydrobenzopyridoazepinyl-N-carbonylamino" in the definition of G. There is insufficient antecedent basis for this limitation in the claim.

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- ao) Claim 36 recites the limitation "1,2,4,5-tetrahydrobenzo[d]azepin-3-yl" in the third species. There is insufficient antecedent basis for this limitation in the claim.
- ap) Claim 36 recites the limitation "1H,3H-benzo[d,e]isoquinolin-2-yl" in the seventh species. There is insufficient antecedent basis for this limitation in the claim.
- aq) Claim 36 recites the limitation "10,11-dihydrodibenzo[b,f]azepin-5-yl" in the eighth species. There is insufficient antecedent basis for this limitation in the claim.
- ar) Claim 36 recites the limitation "1,1-dioxo-1-thia-2-aza-acenaphthylen-2-yl" in the ninth species. There is insufficient antecedent basis for this limitation in the claim.
- as) Claim 36 recites the limitation "imidazol-1-yl" in the twelfth species. There is insufficient antecedent basis for this limitation in the claim.
- at) Claim 36 recites the limitation "benzhydrylmethylamino" in the seventeenth species. There is insufficient antecedent basis for this limitation in the claim.
- au) Claims 39-46 recite the limitation "the method of claim..." in each of the claims. There is insufficient antecedent basis for this limitation in the claim. Claim 37 is a composition claim not a method claim.
- av) Claim 46 recites the limitation "2, ... 20, ..., 30, 50, 75, 100, 200, 300, 400, 500, 600 or 800" in the dosage units. There is insufficient antecedent basis for this limitation in the claim.
- aw) Claim 46 is vague and indefinite in that it is not known what is meant by the second occurrence of 2 in the dosages.

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- ax) Claim 50 is vague and indefinite in that it is not known what is meant by the variables R^8 , R^9 , R^{10} and m which are not defined in the claim.
- ay) Claim 50 is vague and indefinite in that it is not known what is meant by the two different definitions for X in the claim.
- az) Claim 50 recites the limitation "ring systems $=CR^8R^9$ " in the definition of the substitutions on the aromatic rings. There is insufficient antecedent basis for this limitation in the claim.
- ba) Claim 51 is vague and indefinite in that it is not known what is meant by the variables X and n which are not defined in the claim.
- bb) Claims 51 and 54 are vague and indefinite in that it is not known what is meant by the definition of Ar^1 and Ar^2 in the claim. There are no variables Ar^1 and Ar^2 in the claim.
- bc) Claim 51 is vague and indefinite in that it is not known what is meant by the definition of the substituents on the aromatic rings of R^{11} , R^{12} , Ar^1 and Ar^2 and in the ring system $=CR^8R^9$. There are no variables R^{11} , R^{12} , Ar^1 and Ar^2 and the ring system $=CR^8R^9$ in the claim.
- bd) Claim 52 is vague and indefinite in that it is not known what is meant by the variables R_{12} which is not defined in the claim.

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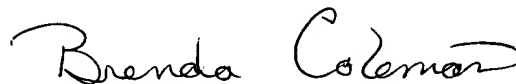
- be) Claims 52-54 are vague and indefinite in that it is not known what is meant by the definitions of m , R^8 , R^9 , R^{10} and R^{11} which is “can have the above meaning”.
However, they are not defined within the claim.
- bf) Claim 52 is vague and indefinite in that it is not known what is meant by the definition of R^{11} which is “has the above meaning”. However, it is not defined within the claim.
- bg) Claim 52 is vague and indefinite in that it is not known what is meant by the definition of X which is “has the above meaning”. However, it is not defined within the claim.
- bh) Claims 52-54 are vague and indefinite in that it is not known what is meant by the definition of the substituents on the aromatic rings of R^8 , R^9 , R^{10} and R^{11} and the ring system $=CR^8R^9$ which are not defined within the claim.
- bi) Claims 53 and 54 are vague and indefinite in that it is not known what is meant by the definition of G such that there is no indication where the point of attachment is for the moiety.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays from 8:30 AM to 5:00 PM, on Tuesdays from 8:00 AM to 4:30 PM, on Wednesday thru Friday from 9:00 AM to 5:30 PM.

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The fax phone number for this Group is (703) 308-4734 for “unofficial” purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

A handwritten signature in cursive script that reads "Brenda Coleman".

Brenda Coleman
Primary Examiner AU 1624
November 18, 2002